Chemotherapeutic Role of Aqueous Extract of *Mentha arvensis* against 4-NQO-Induced Oral Carcinogenesis in Murine Model

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Abstract

Conventional cancer treatments mostly have noteworthy side effects, highlighting the need for alternatives. Plant-derived bioactive compounds are emerging as promising cancer therapies. This study explores the chemotherapeutic potential of aqueous extract of Mentha arvensis (AEMA) in a Swiss albino mice model of oral cancer induced by 4-nitroquinoline-1-oxide (4NQO). Significant differences in body weight were recorded during the treatment process. The control group exhibited a 56% increase in body weight, while the 4NQO-treated group showed a 16% gain, indicating marked toxicity. Mice treated with 4NQO followed by Mentha arvensis extract (AEMA) demonstrated a 35% increase in body weight, suggesting a protective effect. Histopathological analysis of the 4NQO-only group revealed moderate to severe dysplasia, with tumor cells infiltrating skeletal muscle fibers.

In contrast, the AEMA-treated group showed mild dysplasia, a reduced risk of oral carcinoma and lower tumor burden. AEMA also significantly mitigated oxidative stress, as evidenced by reduced levels of TBARS ($p<0.001$) and restored SOD activity ($p<0.001$) in the tongue tissue. These findings indicate that AEMA is crucial in alleviating 4NQO-induced oxidative damage. The results support the potential of Mentha arvensis as a promising chemotherapeutic agent for reducing tumor progression and enhancing antioxidant defenses in oral cancer.

Keywords: Antioxidant activity, Chemotherapeutic potential, *Mentha arvensis*, Oral cancer, 4-nitroquinoline-1-oxide (4NQO)

Introduction

Cancer is a multifaceted disease characterized by uncontrolled cell division, necessitating various approaches for prevention and treatment. Squamous cell carcinoma (SCC) of the oral cavity is one of the most common forms, accounting for about 90% of oral cancers. This type, known as oral squamous cell carcinoma, often spreads via metastasis, with the tongue being the most frequently affected site[17]. Conventional treatments are widely used but come with substantial side effects. In advanced cases, surgery may cause speech difficulties, problems with chewing or swallowing and facial disfigurement. Due to these limitations, many people are turning to ethnobotanical remedies which are generally better tolerated and have fewer side effects. These natural treatments, rich in antioxidants, are particularly beneficial for long-term use or chronic conditions[32].

The 4-nitroquinoline-1-oxide (4NQO) model is commonly used to induce experimental oral carcinogenesis, particularly on the tongue. As a synthetic, water-soluble carcinogen, 4NQO promotes DNA adduct formation and oxidative stress, leading to molecular and systemic damage. This model closely mimics the stages of human oral cancer development including hyperplasia, dysplasia and carcinoma *in situ*[6]. 4NQO is metabolized into 4-hydroxyaminoquinoline oxide (4-HAQO) which generates hydrogen peroxide and depletes glutathione, thereby causing oxidative damage[18]. Reactive oxygen species (ROS) disrupt the balance with antioxidants, leading to oxidative stress. The oral cavity, due to the rapid absorption of chemicals through the mucosal membrane, is particularly vulnerable to oxidative damage[16].

One of the key factors contributing to cancer development is the overproduction of reactive oxygen and nitrogen species. Phytochemicals found in fruits, vegetables and grains may offer protection against cancer, primarily due to their antioxidant properties. Research suggests that dietary factors contribute to over 35% of cancer-related deaths and lifestyle changes could prevent nearly two-thirds of cancer cases. Free radicals, such as lipid peroxidation and peroxyl radicals, can induce DNA mutations that initiate carcinogenesis. Antioxidant-rich phytochemicals have the potential to withstand these carcinogenic processes[11].

Mentha arvensis, is known for its use in folk medicine to treat conditions like fever, colds, spleen, asthama, liver ailments and digestive issues[28]. Apart from this, the plant is used in aromatherapy and in the past few years, its pharmacological qualities, such as its ability to treat certain diseases and disorders, have gained attention, including its antidiabetic, anti-cytotoxic, antioxidant and antibacterial properties[23]. According to Yuan et al[34], the presence of a significant quantity of substances originating from nature, such as polyphenols, carotenoids, compounds containing sulfur, terpenoids, flavonoids, phenolic acids, etc. suggests that a plant may be a good candidate for anticancer therapy[34]. *Mentha arvensis* has played a more progressive role in cancer research in recent years, but it is still restricted to a few cancer types, with oral cancer still being excluded.

Therefore, the present work is dedicated to the anticancer activity of aqueous extract of *Mentha arvensis* in a 4NQO-induced oral cancer mice test model.

Material and Methods

Plant Material: *M. arvensis* fresh leaves were collected from Panivoral village in the Biswanath district, Assam, India. The plant materials (Collection number: PD003) have been verified by Assam University Silchar Central Herberium, Silchar, Assam, India. The Department of Life Science and Bioinformatics, Assam University, Silchar, Assam, India, received the herbarium sheet of *M. arvensis* (accession number 0080003).

Ethical Statement: According to the guidelines established by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Swiss albino mice were kept in the animal house of the Department of Life Science and Bioinformatics. The Institutional Animal Ethics Committee (IAEC) of Assam University, Silchar has approved the experimental work; the approval number is AUS/IAEC/PD-R(a)/2023-1/014.

Preparation of plant extract: Fresh *Mentha arvensis* leaves were washed with double-distilled water, shade-dried and crushed into a coarse powder. The powder was macerated in 200 ml of aqueous solvent for three days in an airtight container with periodic shaking[30]. After maceration, the mixture was filtered using Whatmann no.1 filter paper and the filtrate was lyophilized to obtain the crude extract. The extract was stored at -20°C and dissolved in double-distilled water before use, within one month[2].

Dose selection and study design: The LD50 (Lethal Dose, 50%) for the selected plants was established through the limit test in accordance with OECD guidelines-425. Upon evaluation, it was inferred that the LD50 for the selected plant extract exceeds 2000 mg/kg body weight. Thereafter, a dose of 400mg/kg BW of aqueous extract of *Mentha arvensis* (AEMA) was chosen and administered orally during the treatment[10,12].

In this work, 30 Swiss albino mice of both sexes were taken and distributed into 5 experimental groups (n=6) (Figure 1). Group 1(n=6) served as the control, receiving only a basal diet and tap water throughout the period. Group 2 was exposed to 4-nitroquinoline 1-oxide (4NQO), dissolved in propylene glycol. At 8 weeks of age, mice in group 2(n=6) were topically administered 0.5% 4NQO in propylene glycol at 5mg/ml conc., in aliquots of 25µl with camel brush no. 3 on the tongue[6], thrice per week for 16 weeks. Group 3 (n=6), the vehicle control, received propylene glycol alone for the same period. In group 4 (n=6), mice were administered 400 mg/kg BW of AEMA, starting from week 18, after the cessation of 4NQO exposure till 32 weeks. Group 5 (n=6) received curcumin, as a standard comparator, in place of the plant extract following the completion of 4NQO treatment.

Change in body weight: The initial and final body weights were considered for the observation of changes in the body weight of model organisms in each group. The change in body weight is denoted in percentage and is calculated as:

$$\%\ Body\ Weight\ Change = \frac{(final\ body\ weight\ -\ initial\ body\ weight)}{initial\ body\ weight}\ X\ 100$$

Change in tongue Morphology and Histology: Following dissection, the tongues of the mice were thoroughly inspected for any morphological changes. The tongue samples were then carefully processed for histopathological studies. The fixed tissues were subjected to dehydration and subsequently embedded in paraffin. Thin sections of 5 µm in thickness were cut from the paraffin blocks and mounted on slides. To evaluate histological changes, the sections were rehydrated using a series of graded alcohols and then stained with haematoxylin and eosin. The slides were then examined under a light microscope (Leica DMLS) and images of relevant areas were captured at the appropriate magnifications (10X or 20X).

Lipid peroxidation: Lipid peroxidation (LPO) in tongue tissues was evaluated by measuring thiobarbituric acid-reactive substances (TBARS)[21]. A 10% tissue homogenate was prepared in ice-cold physiological saline and centrifuged at 3000 rpm for 10 minutes. From the supernatant, 1 ml was collected, incubated at 37°C for 2 hours, then mixed with an equal volume of 10% (w/v) trichloroacetic acid and centrifuged at 2000 rpm for 5 minutes at 4°C.

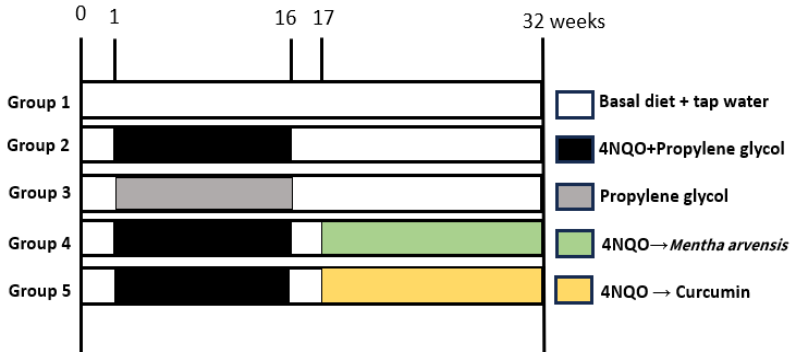

Figure 1:Treatment design for different groups.

Subsequently, 1 ml of the resulting supernatant was combined with 1 ml of 0.67% (w/v) thiobarbituric acid and incubated in a water bath for 10 minutes, followed by dilution. The optical density (OD) was measured at 535 nm using a Genesys-20 spectrophotometer (Thermo Scientific, USA) and results were expressed in nmol/g of wet tissue.

Reduced glutathione assay (GSH): In the tongue tissues, reduced glutathione levels were determined using the 5,5'-dithiobis-2-nitrobenzoic acid (DTNB) method[25]. Tissue homogenates were prepared in 0.02 M EDTA, to which 2 ml of ice-cold distilled water was added. Afterwards, 1 ml of 50% (w/v) trichloroacetic acid was added followed by centrifugation at 6000 rpm for 15 minutes. From the resulting supernatant, 1 ml was taken and mixed with 2 ml of Tris buffer (0.4 M; pH 8.9) and 100 µl of 0.1 M DTNB. The optical density was measured at 410 nm and glutathione levels were expressed in µmol/g of wet tissue.

Superoxide dismutase (SOD) activity: Superoxide dismutase (SOD) activity in tongue tissues was evaluated using the protocol established by Marklund and Marklund[14]. A 10% tissue homogenate was prepared in ice-cold physiological saline and centrifugation was performed at 3000 rpm for 10 minutes. From the supernatant, 100 µl was combined with 2900 µl of Tris-HCl buffer (pH 8.5), achieving a total volume of 3 ml. Following this, 25 µl of 24 mM pyrogallol was added and the mixture was thoroughly mixed and incubated for 1 minute. The absorbance was then measured at 420 nm at 1-minute intervals for a total duration of 3 minutes.

Statistical analysis: SPSS version 21.0 (IBM Corp., Armonk, New York) was used for statistical analysis and GraphPad Prism version 8.0 (GraphPad Software, San Diego, California, USA) at a 95% confidence interval (CI). One-way analysis of variance (ANOVA) was employed followed by Tukey's multiple comparison test for pairwise comparisons among the study groups. Statistical significance was at $p < 0.05$.

Results

Change in body weight: After treatment, body weight changes in the treatment groups showed significant differences when compared to the control group (Table 1). The control group exhibited an approximate 56% increase in body weight, while the propylene glycol group showed a similar increase of around 47%. In stark contrast, the 4NQO group displayed a modest gain of only 16%. However, the 4NQO→AEMA group demonstrated a notable 35% increase in body weight and the 4NQO→Cur group exhibited an approximate 45% increase. Importantly, the group exposed solely to 4NQO showed significant impairment in body weight, whereas the groups treated with plant extracts and curcumin following 4NQO administration effectively maintained more favorable weight outcomes. These results depict interventions with AEMA and curcumin may mitigate the adverse effects of 4NQO on body weight.

Change in tongue morphology and histology: The tongues of control mice and those treated with propylene glycol (PPG) exhibited no morphological alterations, appearing normal post-treatment (Figure 2). In contrast, all animals in the 4NQO-treated group developed the tumor nodules, resulting in a tumor burden of 100% across the group. However, mice receiving 4NQO→AEMA and 4NQO→Cur treatments displayed a marked reduction in tumor burden compared to the 4NQO group. Notably, little to no significant differences in tumor volume or burden were observed in the 4NQO→AEMA and 4NQO→Cur study groups. These findings indicate that both AEMA and curcumin effectively reduce tumor burden associated with 4NQO exposure, highlighting their potential as therapeutic agents.

Histopathological analysis revealed that tongue tissue from mice exposed solely to 4NQO exhibited moderate to severe dysplasia, characterized by high-grade dysplastic cells and tumor cells infiltrating skeletal muscle fibers (Figure 3). There were significant variations in the basement membrane, lacking a well-defined epithelial boundary.

In contrast, the curcumin-treated group demonstrated a lower risk of carcinoma compared to the 4NQO-only group, with indications of partial restoration of the basement membrane. Mice treated with various plant extracts (4NQO → AEMA) displayed only mild dysplasia, indicating a reduced risk of oral carcinoma and fewer carcinogenic changes relative to the untreated groups.

Table 1
Body weight changes observed in mice

Groups	Initial weight (grams)	Final weight (grams)	Change in weight gain (grams)	% Change
Control	21.58±1.64	33.53±3.33	11.95±3.96	56.34±4.41
4NQO	21.43±1.22	24.85±1.02	3.42±2.00	16.36±3.77
Propylene glycol (PPG)	20.93±1.18	31.03±4.23	10.10±3.24	47.84±5.89
4NQO+ *Mentha arvensis*	21.52±1.37	29.42±2.98	7.90±2.06	36.59±5.68
4NQO+ Curcumin	20.47±1.00	29.77±2.77	9.3±2.57	45.53±4.58

CON; Control, 4NQO; 4-nitroquinoline 1-oxide, PPG; Propylene glycol, AEMA; Aqueous extract of *Mentha arvensis*, Cur; Curcumin.

Furthermore, histological findings suggested a dose-dependent reduction in the risk of oral squamous carcinoma in the extract-treated group. The observed inhibition of tumor growth in the oral cavity by AEMA is likely attributed to the bioactive constituents present in these extracts, which possess antiproliferative and anticancer properties.

Biochemical assays for evaluation of oxidative stress: This study examined the impact of AEMA and curcumin on oxidative stress markers in the tongues of mice exposed to 4-nitroquinoline 1-oxide (4NQO) (Table 2). Results demonstrated a significant increase in lipid peroxidation, as indicated by elevated TBARS levels in the 4NQO group compared to controls (0.75±0.3) ($p < 0.001$). Notably, treatment with AEMA (0.54±0.06) and curcumin (0.48±0.07) resulted in a substantial reduction in TBARS levels ($p < 0.001$), suggesting their potential to mitigate oxidative stress (Figure 4). Additionally, glutathione (GSH) levels were significantly higher in the tongues of 4NQO-treated mice compared to the control group (0.156±0.01) ($p < 0.001$).

However, those treated with AEMA (0.0135±0.02) and curcumin (0.128±0.02) exhibited a marked reduction in GSH levels, indicating a recovery from oxidative stress (Figure 5). Similarly, superoxide dismutase (SOD) levels significantly decreased in the 4NQO (1.19±0.19) group relative to controls ($p < 0.001$) whereas treatment with AEMA (4.76±0.23) and curcumin (4.56±0.20) resulted in significant increases in SOD levels ($p < 0.001$) (Figure 6). Collectively, these results suggest that AEMA and curcumin effectively alleviate oxidative stress in the tongue following exposure to 4NQO.

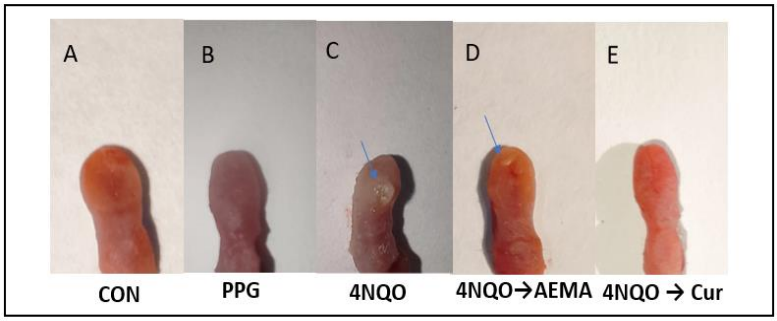

Figure 2: Therapeutic effect of aqueous leaf extract of *Mentha arvensis* (AEMA) and Curcumin against 4NQO-induced tumor formation in tongue morphology of mice. CON; Control, 4NQO; 4-nitroquinoline 1-oxide, PPG; Propylene glycol, AEMA; Aqueous extract of *Mentha arvensis*, Cur; Curcumin.

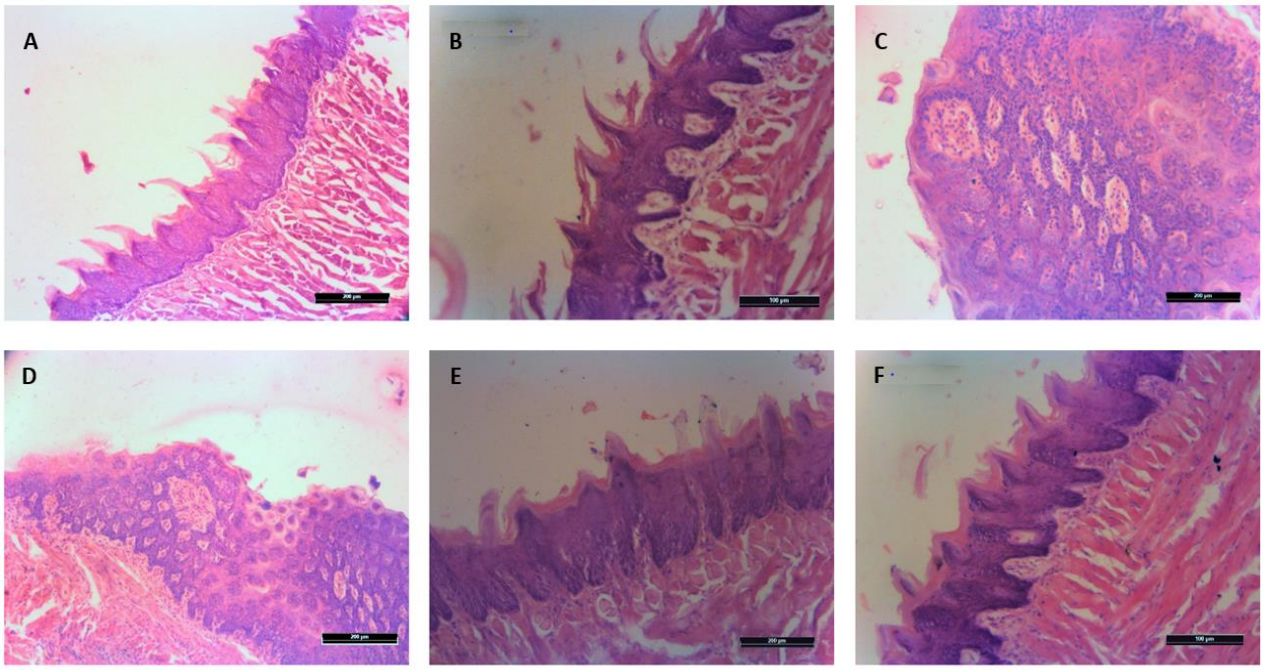

Figure 3: Histopathological examination of 4-NQO-induced neoplastic changes in tongue tissues of mice in different experimental groups. (A) Control 10X- normal epithelium; (B) PPG 20X-normal epithelium; (C) 4NQO 20X- severe dysplasia/carcinoma in situ; (D) 4NQO 10X- moderate dysplasia; (E) 4NQO→AEMA 20X- mild hyperplasia; (F) 4NQO→Cur 20X-mild hyperplasia. 4NQO; 4-nitroquinoline 1-oxide, PPG; Propylene glycol, AEMA; Aqueous extract of *Mentha arvensis*, Cur; Curcumin.

Table 2
Biochemical estimation of TBARS content, GSH level and SOD activity in tongue of Swiss albino mice

Treatment groups	TBARS (nmol/g tissue)	GSH (µmol/g tissue)	SOD (Units/min)
Control	0.43±0.03	0.99±0.01	5.07±0.33
4NQO	0.75±0.04	0.156±0.01	1.19±0.19
PPG	0.47±0.04	0.110±0.01	4.96±0.35
4NQO→AEMA	0.54±0.06	0.135±0.02	4.76±0.23
4NQO→Cur	0.48±0.07	0.128±0.02	4.56±0.20

CON; Control, 4NQO; 4-nitroquinoline 1-oxide, PPG; Propylene glycol, AEMA; Aqueous extract of *Mentha arvensis*, Cur; Curcumin.

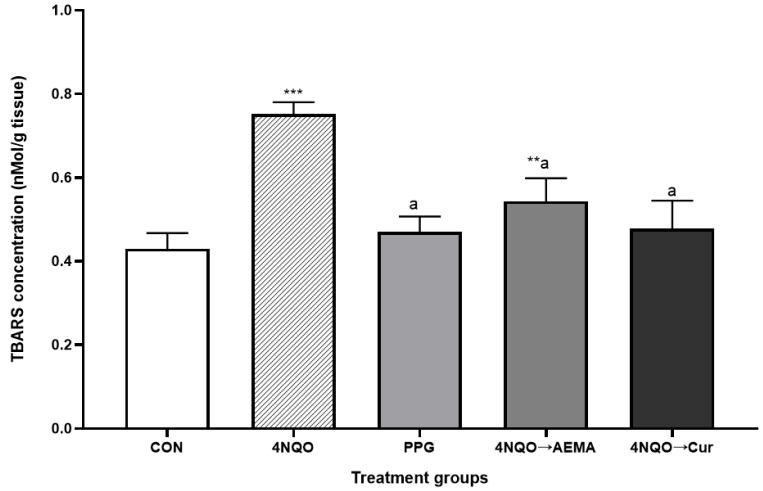

Figure 4: Histogram showing the concentration of oxidative stress marker TBARS in different treatment groups. CON; Control, 4NQO; 4-nitroquinoline 1-oxide, PPG; Propylene glycol, AEMA; Aqueous extract of *Mentha arvensis*, Cur; Curcumin. Each bar indicates the mean of six experimental animals (n=6) and error bars indicated SD. Statistical analysis: One-way analysis of variance (ANOVA) followed by Tukey's test for multiple comparisons. *indicates values are significantly different from control at p<0.05(*), p<0.01(**) and p<0.001(***). 'a' indicates values are significantly different from 4NQO.

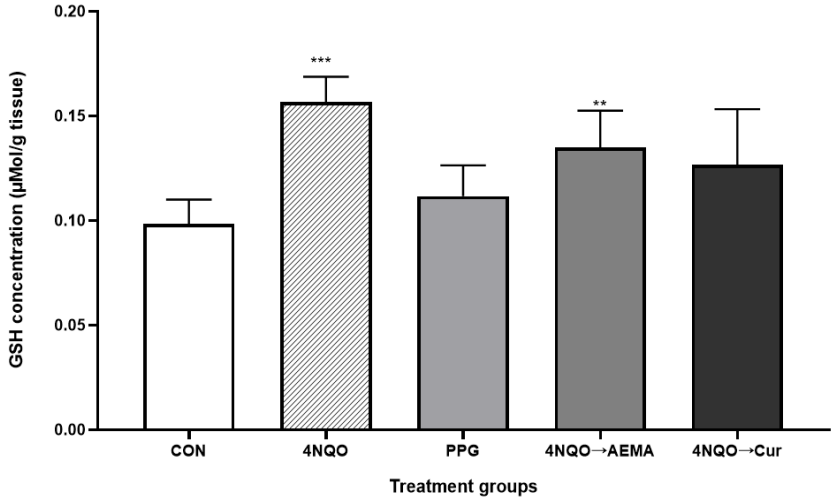

Figure 5: Histogram showing the concentration of oxidative stress marker GSH in different treatment groups. CON; Control, 4NQO; 4-nitroquinoline 1-oxide, PPG; Propylene glycol, AEMA; Aqueous extract of *Mentha arvensis*, Cur; Curcumin. Each bar indicates the mean of six experimental animals (n=6) and error bars indicated SD. Statistical analysis: One-way analysis of variance (ANOVA) followed by Tukey's test for multiple comparisons. *indicates values are significantly different from control at p<0.05(*), p<0.01(**) and p<0.001(***). 'a' indicates values are significantly different from 4NQO.

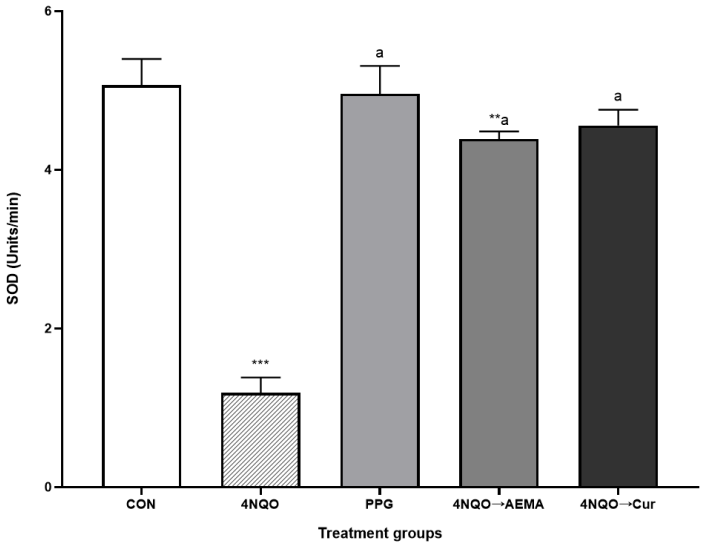

Figure 6: Histogram showing the concentration of oxidative stress marker SOD in different treatment groups. CON; Control, 4NQO; 4-nitroquinoline 1-oxide, PPG; Propylene glycol, AEMA; Aqueous extract of *Mentha arvensis*, Cur; Curcumin. Each bar indicates the mean of six experimental animals (n=6) and error bars indicated SD. Statistical analysis: One-way analysis of variance (ANOVA) followed by Tukey's test for multiple comparisons. *indicates values are significantly different from control at p<0.05(*), p<0.01(**) and p<0.001(***). 'a' indicates values are significantly different from 4NQO.

Discussion

The use of natural products such as green tea and fruit or vegetable extracts from sources like grapes, apples and tomatoes, has gained attention for the prevention and treatment of oral cancer. In relation to this, animal models are critical for studying disease progression and developing diagnostic and therapeutic protocols[7,9,22,26]. However, the antitumor activity of AEMA, on oral cancer has been previously not reported. In this study, we employed a 4NQO-induced oral cancer model to assess the therapeutic effectiveness of AEMA.

Previous studies have confirmed that rats exposed to 4NQO at 20 ppm for 10 weeks showed a reproducible incidence of squamous cell carcinoma (SCC) in the tongue, with an 83% incidence rate after 26 weeks[20]. The extent and nature of dysplastic and neoplastic lesions induced by 4NQO depend on both the duration and dose of exposure, leading to molecular and morphological changes that closely resemble human carcinogenesis[27]. In the existing study, the administration of 4NQO at 5mg/ml conc., in aliquots of 25µl for oral painting, resulted in precancerous and cancerous morphological changes in the tongue epithelium after 16 weeks.

4NQO exposure is also connected with gradual weight loss in animal models, linked to oral cancer development, reduced appetite, feeding difficulties and increased metabolic rate[29]. Coinciding with these reports, our study observed a substantial reduction in body weight in the cancer-induced group. However, treatment with a 400mg/Kg BW dose of AEMA significantly mitigated this weight loss, suggesting its potential role in reducing the adverse effects associated with oral cancer. The role of free radicals in lipid peroxidation and the involvement of antioxidants in carcinogenesis are well established[4]. In 4NQO-induced oral tumors, susceptibility to lipid peroxidation notably increased compared to adjacent non-tumorous tissue and the oral mucosa of control animals. Previous studies like that of the evaluation of ethyl acetate fraction of *Mentha spicata* on 4NQO injected mice by Arumugam and Ramesh[1] have also shown 1.6 levels of increased LPO by 4NQO compared to control. Our present work in in line with this study as it is significant.

Earlier examination of the activities of intracellular antioxidant enzymes revealed significant alterations. SOD activities were diminished in 4NQO-induced tumor tissues compared to normal mucosa, while glutathione peroxidase activity was evidently elevated. Low SOD and catalase activity are general features of rapidly growing tumors[3,19], as the reduction of these enzymes is characteristic of cellular transformation. Glutathione, a crucial substrate for glutathione peroxidase, plays a regulatory role in cell proliferation[15]. Overexpression of glutathione has been observed in malignant tumors [5] and raised up levels have been seen in several tumor tissues and cell lines[5,33]. However, few studies have specifically examined glutathione levels in experimental models of oral carcinogenesis. In this study, elevated glutathione activity in oral cancer tissues may indicate markers of increased cell proliferation.

The existing study depicts that treatment with plant extracts, particularly AEMA and curcumin, significantly mitigated the adverse effects of 4NQO-induced oral carcinogenesis in mice. Body weight analysis revealed distinct differences across treatment groups. While the control group exhibited

an approximate 56% increase in body weight, the 4NQO group showed a markedly lower gain of 16%, reflecting visible impairment caused by 4NQO administration. In contrast, treatment with AEMA and curcumin improved body weight retention, with increases of 35% and 45% respectively, highlighting their potential protective effects. These findings align with prior studies, such as those by Mohan et al[17] who reported similar weight preservation during the evaluation of ethyl gallate's anticancer properties.

Histopathological analysis further substantiates the chemopreventive effects of these plant extracts. Mice treated with 4NQO alone developed significant tumor burdens, with 100% of animals showing extensive tumor nodules and severe dysplasia. In contrast, groups treated with AEMA and curcumin exhibited substantial reductions in tumor burden, with mild dysplasia and lower carcinoma risk. These findings are in alignment with previous work by Al-Koshab who observed the antitumor activity of *Ficus deltoidea* extract on oral cancer.

Moreover, the histological results demonstrated a dose-dependent reduction in oral squamous carcinoma, suggesting that the bioactive constituents in AEMA may play a crucial role in inhibiting tumor progression, in line with studies by Schoop et al[24] and Luo et al[13].

Biochemical analyses supported these morphological findings. Lipid peroxidation, measured by TBARS conc., was significantly raised in 4NQO-induced mice, indicating heightened oxidative stress. However, treatment with AEMA and curcumin significantly reduced TBARS levels ($p<0.001$), suggesting that these extracts effectively attenuated oxidative damage. These results are consistent with the observations of Mohan et al[17] and Upadhaya[31] who also noted reductions in oxidative stress markers in their respective studies on ethyl gallate and *Mikania micrantha* extracts. Glutathione (GSH) levels were similarly impacted. GSH conc. were significantly increased in 4NQO-induced mice, reflecting the oxidative burden.

Treatment with AEMA and curcumin resulted in a marked reduction in GSH levels ($p<0.001$), indicative of oxidative stress recovery. Similar trends were reported by Droguett et al[8] and Das et al[6] in their investigations of neem leaf glycoprotein and its immunomodulatory effects on 4NQO-induced oral carcinogenesis. Superoxide dismutase (SOD) activity, which was significantly reduced in the 4NQO-induced group, was restored following treatment with AEMA and curcumin ($p<0.001$), underscoring their antioxidative efficacy.

These results, comparable to those of Mohan et al[17] and Upadhaya[31], further reinforce the therapeutic potential of these plant extracts in mitigating oxidative stress and reducing tumorigenesis in oral cancer models. Overall, these findings highlight the potential chemotherapeutic properties of AEMA and curcumin in managing 4NQO-induced oral carcinogenesis, likely due to their antioxidative and antiproliferative effects.

The changes in antioxidant levels observed in 4NQO-induced oral tumors reflect a combination of malignant transformation and cell division. Treatment with AEMA and Curcumin was able to reverse these oxidative changes, supporting the theory that certain plant-based antioxidant phenolics function as blocking agents in the prevention of oral cancer.

Natural dietary phytoconstituents will continue to be a key area of research, with future studies needed to explore plant-derived phytochemicals, focusing on their therapeutic potential, mechanisms of action, pharmacokinetics, metabolism, pharmacodynamics, toxicity, polymorphisms and drug interactions. Establishing proper dosage routines for their use as standard herbal medicines is crucial. Large-scale, well-controlled clinical trials are essential to evaluate their efficacy, safety and side effects. Additionally, furture research should explore the synergistic effects of combining phytochemical compounds with chemotherapeutic drugs in cancer treatment.

Conclusion

In conclusion, this study highlights the potential of natural dietary phytoconstituents, particularly *Mentha arvensis* and its comparison with Curcumin, in mitigating the adverse effects of 4NQO-induced oral carcinogenesis. The findings suggest that these plant-based compounds exhibit significant antioxidative and antiproliferative properties, as demonstrated by improved body weight retention, reduced tumor burden and restored antioxidant enzyme activity in treated animals.

The results underscore the importance of continued research on phytochemicals, focusing on their mechanisms of action, pharmacokinetics and synergistic effects with chemotherapeutic agents. Future large-scale clinical trials are necessary to thoroughly explore their therapeutic potential and establish their role in oral cancer prevention and treatment.

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